REMARKS

I. Status of Claims

Claims 1-25 and 34-36 were pending at the time of the Final Office Action (herein after FOA). Claims 1-4, 13, 15, 18, 19, 21-24 and 34-36 have been amended without prejudice or disclaimer. Applicants reserve the right to prosecute any amended or deleted matter in one or more continuation applications. No new matter has been added by the claim amendments. Support for amended claims can be found in the originally-filed specification at least on page 40, line 15 through page 43, line 5. Accordingly, claims 1-25 and 34-36, as amended, are now pending in the application.

II. Claim Objections

The Examiner objected to claims 1-4, 13, 15, 18, 21-24 and 34-36 because of informalities for not reciting the phrase "magnetic" consistently while reciting "first/second" "particulate solid supports." Applicants present amended claims 1-4, 13, 15, 18, 19, 21-24 and 34-36 which now overcome the claim objections.

III. Specification Objection

The Examiner objection to amendment to specification filed on October 27, 2010 under 35 U.S.C. §132(a) because it introduces new matter into the disclosure.

Applicants amended claims 1-4, 13, 15, 18, 19, 21-24 and 34-36 now do not recite "plurality of" while describing the "first," "second," and "third" supports. Accordingly, Applicants respectfully submit that the objections to the specification are now overcome.

IV. Rejections under 35 U.S.C. § 112, First Paragraph

The Examiner rejected claims 1-25 and 34-36 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description for containing new matter and claim interpretation.

Applicants have presented amended claims 1-4, 13, 15, 18, 19, 21-24 and 34-36 which now overcome the new matter and claim interpretation related written description rejections.

Amended claims are supported in the originally-filed specification at least on page 40, line 15 through page 43, line 5. In view of the amendment to claims, Applicants respectfully request withdrawal of the instant rejections under 35 U.S.C. §112, first paragraph, written description requirement and request allowance of claims 1-25 and 34-36.

V. Rejections under 35 USC § 103(a)

A. Claims 1-25 and 34 stand rejected as allegedly being unpatentable over U.S. Patent No. 6,255,477 to Kleiber et al. ("Kleiber") in view of U.S. 6,723,510 to Lubenow ("Lubenow") and further in view of Schubler et al. (TIG, 1995, 11, 378-379) ("Schubler").

Applicants respectfully traverse this rejection. According to the M.P.E.P. § 2143.03, a threshold requirement for establishing a *prima facie* case of obviousness is that all elements of the claim or claims rejected must be found in the combination of references cited, *i.e.*, combination of Klieber, Lubenow and Schubler, and there must be a clear reasoning as to why such a combination would produce the results of the presently claimed embodiments. In addition, when "an independent claim is nonobvious under 35 U.S.C. § 103, then any claim depending therefrom is nonobvious." Furthermore, in accordance to Federal Circuit jurisprudence, the mere assertion of obviousness does not establish a *prima facie* case of obviousness. In deriving this inference, the Final OA ("FOA") is evidently proceeding with an impermissible "hindsight analysis" of the invention. This is clearly improper under the law. To imbue one of ordinary skill in the art with knowledge of the instant invention, where no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher. *W.L. Gore Assoc., Inc. v. Garlock, Inc.*, 220 USPQ 303, 312-313 (Fed. Cir. 1983).

For example, as acknowledged by the Examiner, on page 8 of the FOA, "Kleiber does not teach explicitly the binding proteins to the second magnetic particulate solid supports by effecting a chromatographic interactions and separating the plurality of first magnetic particulate supports and the second magnetic particulate supports bound to the proteins from unbound components in the sample."

In addition, Klieber fails to teach or suggest at least the following elements of currently amended independent claim 1, from which all other pending claims 2-25 and 34 are dependent, including: "contacting the sample with a plurality of magnetic particulate solid supports comprising: contacting said sample with a first magnetic particulate solid support wherein nucleic acid components bind to the first magnetic particulate solid supports in a sequence independent manner;" "contacting the sample with a second magnetic particulate solid support distinct from the first magnetic particulate solid support, wherein protein components contained in the sample bind to the second magnetic particulate solid support through a chromatographic interaction;" and "separating the first magnetic particulate solid support to which are bound nucleic acid components and the second magnetic particulate solid supports to which are bound protein components from unbound components in the sample."

Applicants have failed to find in Klieber any teaching or suggestion of:"contacting the sample with a second magnetic particulate solid support distinct from the first magnetic particulate solid support, wherein protein components contained in the sample bind to the second particulate solid support through a chromatographic interaction;" and "separating the first magnetic particulate solid support to which are bound nucleic acid components and the second magnetic particulate solid supports to which are bound protein components from unbound components in the sample." The FOA also appears to acknowledge that these elements are missing in Klieber. Accordingly, the combination of Klieber with the other cited references appears to be no more than a "hindsight analysis" of the claimed embodiments.

Lubenow fails to teach or suggest the missing elements of Klieber. For example Lubenow fails to teach or suggest at least the following elements of currently amended independent claim 1, from which all other pending claims 2-25 and 34 are dependent, including: "contacting the sample with a plurality of magnetic particulate solid supports comprising: contacting said sample with a first magnetic particulate solid support wherein nucleic acid components bind to the first magnetic particulate solid supports in a sequence independent manner;" "contacting the sample with a second magnetic particulate solid support distinct from the first magnetic particulate solid support, wherein protein components contained in the sample

bind to the second magnetic particulate solid support through a chromatographic interaction;" and "separating the first magnetic particulate solid support to which are bound nucleic acid components and the second magnetic particulate solid supports to which are bound protein components from unbound components in the sample."

For example, although the FOA alleges that Lubenow teaches the separation of both nucleic acids and proteins from a sample using magnetic particles (see lines adjoining pages 8 and 9 of the FOA), Applicants respectfully submit that Lubenow fails to teach the claimed embodiments of the present disclosure as recited in currently amended claim 1 above. For example, Lubenow fails to teach or suggest the separation of both nucleic acid and protein components of a sample in a single method (which is also not taught or suggested by Klieber).

Furthermore, with respect to nucleic acids, in the sections referenced by the FOA, Lubenow appears to teach no more than using "oligo dT magnetic particles for binding polyA RNA (see Column 5, lines 38-67 and column 6, lines 1-27 of Lubenow). Lubenow utterly fails to teach or suggest at least the following element of currently amended claim 1 with recites with respect to nucleic acids: "nucleic acid components bind to the first magnetic particulate solid supports in a sequence independent manner" (emphasis added by underlining).

In addition, with respect to purifying a protein from a sample, Lubenow fails to teach or suggest purifying any protein that has no "affinity tag" for example, see abstract which only recites "affinity particles or beads" (see Abstract of Lubenow) and see the claims which appear to claim no more than isolating "fusion proteins" "consisting of a plurality of consecutive histidine residues" (see all claims of Lubenow). This is further evidenced in column 5 lines 38-62 that describe "affinity tags" (see reproduced below); column 6, lines 27-51 that appear to describe no more than fusion proteins and "His-tagged protein;" and furthermore in the entire section of Examples located at column 13, lines 35 through column 20 line 2, which appear to describe purifying no more than fusion proteins with affinity tags (polyhistidine). Some of these sections are reproduced below for the convenience of the Examiner.

Lubenow, in column 5 lines 38-62 recites:

> The term **"affinity particle" is used to describe any particle bearing an affinity ligand that is capable of binding (forming an affinity complex) with a molecule of interest**. Any affinity ligand may be used that exhibits an acceptable affinity and specificity for the

molecule of interest under the conditions of the contacting step. Such **affinity ligands for use on particulate matrices include**, without limitation, antibodies for a particular antigen, antigens for a particular antibody, antibodies recognizing a class of molecules such as a class of IgG molecules (e.g., anti-human IgG, anti-mouse IgG), streptavidin (or streptavidin-tagged fusion proteins) for binding biotin or biotin-tagged fusion proteins, glutathione for binding GST, cellulose for binding CBD, amylose for binding MBP, ion exchange resins, hydrophobic interaction resins, **oligo-dT for binding poly A tail of mRNA, nucleic acid polynucleotides for binding complementary polynucleotides**, ligands for binding cells (i.e., binding molecules for cell-surface markers), phage ligands, antibodies recognizing cell or phage surface antigens, and any other type of polypeptide, nucleotide or small molecule capable of affinity interactions with a binding partner, whether another protein, DNA, RNA, or small molecule. Specific mention is made of **metal chelate affinity particles**, in particular nickel ion chelate materials, such as nickel-nitrilotriacetic acid (Ni-NTA) coated agarose beads.

(column 5, lines 38-62, Lubenow, **emphasis added**)

Lubenow in column 6 lines 27-51 recites:

The term "**His-tagged protein", "6x-His-tagged protein", or "polyHis-tagged protein" is used to describe a fusion protein in which a protein of interest is fused to a metal chelating group which is a polypeptide segment comprised of a plurality of histidine residues or other chelating amino acids such as cysteine, arginine, or serine, most preferably a segment completely comprised of histidine residues**. Preferably the plurality of histidine residues is at least two or more, most preferably six such residues, forming a "6x-His-tagged" protein. Fusion proteins containing an affinity peptide tag are easily purified from samples including cultures of recombinant eucaryotic and prokaryotic organisms transformed to produce such fusion proteins. The fusion proteins containing an affinity peptide can also be used to assay for a molecule of interest. The affinity of a polyHis tag for copper, nickel, cobalt, or zinc allows the fusion product to be quickly separated from the bulk of other bacterial proteins with up to 95% purity using metal chelate affinity chromatography (Hochuli et al., Bio/Technology, 6: 1321-1325 (1988)). This affinity also allows efficient capturing of a molecule of interest and assaying for its presence in a known or unknown sample. The fusion protein also allows for binding studies, and capture assays. Other affinity tags may also be used and are discussed below.

(column 6, lines 27-51, Lubenow, **emphasis added**)

One of skill in the art, upon review of Lubenow, would agree that Lubenow fails to teach at last the following additional element of claim 1 as currently amended including: "contacting the sample with a second magnetic particulate solid support distinct from the first magnetic particulate solid support, wherein protein components contained in the sample bind to the second magnetic particulate solid support through a chromatographic interaction" (emphasis added by underlining).

One of skill in the art would further agree that neither Lubenow nor Klieber teach or suggest the step of "separating" both protein and nucleic acid as recited in current claim 1.

One of skill in the art, upon review of Klieber, alone or in combination with Lubenow, would agree that, absent the teachings of the present specification, one of skill in the art would not arrive at the teachings of the present claims which recite in independent claim 1.

The Examiner alleges that Schubler teaches use of same sample for protein and nucleic acid isolating at the time of the invention and hence alleges that the combination of Klieber and Lubenow in view of Schubler renders the claims 1-24 and 354 obvious. Applicants respectfully traverse this rejection. Schubler also fails to teach or suggest the elements that are not taught by Klieber and Lubenow.

For example, Schubler, on page 378, in Figure 1 and the description adjoining it, appears to teach no more than separation of "poly A RNA using magnetic ologo$(dT)_{25}$ particles." Schubler fails to teach or suggest at least the following element of currently amended claim 1 which recites: "nucleic acid components bind to the first magnetic particulate solid supports in a sequence independent manner" (emphasis added by underlining). No more than poly A RNA separation using oligo dT columns appear to be taught by Schubler. As shown in sections above these elements are also not taught or suggested by Lubenow.

Furthermore, Schubler fails to teach at least the following additional elements of current independent claim 1 including: "contacting the sample with a second magnetic particulate solid support distinct from the first magnetic particulate solid support, wherein protein components contained in the sample bind to the second particulate solid support through a chromatographic interaction;" and "separating the first magnetic particulate solid support to which are bound nucleic acid components and the second magnetic particulate solid supports to which are bound protein components from unbound components in the sample," (emphasis added by underlining).

Schubler utterly fails to teach protein separation in the same sample using magnetic particles. For example, see Schubler, on page 379 and in Figure 2 which appears to teach no more than purifying proteins from supernatant of the DNA precipitate using buffers that have 2-

mercaptoethanol and SDS. Sections of Schubler describing protein separation are reproduced below:

> Protein can be recovered **either from the supernatant of the CTAB-DNA precipitate or from the supernatant immediately after concentrating the mRNA at the magnet, if DNA is not required**. In both cases, the supernatant and the cell debris pellet from the RNA extraction step were combined. **To extract S. *mansoni* proteins, 1 volume of sample buffer was added (10% vol./vol. glycerol, 5% vol./vol. 2-mercaptoethanol, 3% wt/vol. SDS, 50mM~ Tris-HCl pH 6.8, 5 mM ascorbic acid pH 6.0), the solution was mixed thoroughly , sonicated and then treated as described previous1Y -.J** *A.* thaliana **proteins were extracted by a different procedure without sonication. 1 volume of plant buffer (1OOn-r~N azC03 pH 7.5, 10% saccharose, 50 mu DTE) was added to the supernatant and the cell debris pellet, followed by a 1Omin incubation in sample buffer (2% SDS, 0.1% Bromophenol Blue, final concentration**). The mixture was heated for 30s at 70°C before PAGE. Protein can be concentrated by methanol-chloroform precipitation7 or ulrafiltration (Centrisart I, Sartorius). Protein was evaluated by PAGE and western blotting, and was found to be as equally high in quality as protein obtained by standard methods (Fig. 2).
>
> (Schubler, page 379, second full paragraph, **emphasis added**)

Since the combination of cited references fails to teach or suggest all limitations of claim 1, as amended, a *prima facie* case of obviousness has not been established with respect to claim 1.

Absent all the elements not taught by Klieber, Lubenow and Schubler, the FOA appears to have taken an impermissible "hindsight analysis" of the claimed embodiments. This is clearly improper under the law as analyzed by the Federal circuit which recites: "To imbue one of ordinary skill in the art with knowledge of the instant invention, where no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher." *W.L. Gore Assoc., Inc. v. Garlock, Inc.*, 220 USPQ 303, 312-313 (Fed. Cir. 1983).

One of skill in the art, upon review of Klieber, alone or in combination with Lubenow and/or Schubler, would agree that, absent the teachings of the present specification, one of skill in the art would not arrive at the teachings of the present claims which recite in independent claim 1. Since all dependent claims incorporate by reference the limitations of their independent claims (see 35 U.S.C. §112, ¶4), claims 2-25 and 34 also incorporate by reference at least the elements recited above that are not taught by Klieber in view of Lubenow and Schubler.

Accordingly, at least for analogous reasons, claims 2-25 and 34 are also free of the obviousness rejections.

In view of the evidence above, Applicants respectfully request the withdrawal of rejections under 35 U.S.C. §103(a) and an allowance of claims 1-25 and 34.

B. Claims 35 and 36 stand rejected as allegedly being unpatentable over U.S. Patent No. 6,255,477 to Kleiber et al. ("Kleiber") in view of U.S. 6,723,510 to Lubenow ("Lubenow") and further in view of Schubler et al. (TIG, 1995, 11, 378-379) ("Schubler") and further in view of Petersen (US Patent Application 2001/0012612).

Applicants have already shown in sections above that, one of skill in the art, in view of the teachings of Klieber, alone or in combination with Lubenow and/or Schubler, and absent the teachings of the present specification, would not arrive at the teachings of the present claims which recite in independent claim 1. Since all dependent claims incorporate by reference the limitations of their independent claims (see 35 U.S.C. §112, ¶4), claims 35 and 36 also incorporate by reference at least the elements recited above that are not taught by Klieber in view of Lubenow and Schubler.

Petersen fails to teach the elements recited above that are not taught by the combination of Klieber, Lubenow and Schubler. If indeed such teaching is present, Applicants request the Examiner to provide citation of such a section. Accordingly, at least for analogous reasons, claims 2-25 and 34 are also free of the obviousness rejections.

In view of the evidence above, Applicants respectfully request the withdrawal of rejections under 35 U.S.C. §103(a) and an allowance of claims 35 and 36.

VI. Request for Continues Examination (RCE)

Applicants file concurrently herewith an RCE. Accordingly, entry of the claim amendments presented herein and remarks and evidence are respectfully requested.

VII. Information Disclosure Statement

Applicants file concurrently herewith an IDS to make of record Office Actions and Responses filed in foreign equivalent patent applications and respectfully request review and consideration of these citations.

CONCLUSION

Applicants believe that all outstanding matters in this case have been addresses. In view of the above amendment to claims and remarks, it is submitted that this application and pending claims are now in condition for allowance. Early notice to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (512) 721-3657.

Respectfully Submitted,

/ Priya D. Subramony /
Priya D. Subramony, PhD.
Registration No. 50,939
AGENT FOR APPLICANTS

Date: May 31, 2011
LIFE TECHNOLOGIES CORP.
Direct Dial: 512.944.9198
Customer No. 52059 (L)